REMARKS

Claims 1 and 4-24, as amended, appear in this application for the Examiner's review and consideration. Claims 1 and 14 have been amended to recite that the electrode cartridge is designed for easy attachment to the main unit and subsequent detachment from the main unit, support for which is found in the specification, e.g., paragraph [0066] and the drawings of the published application. Accordingly, claim 3 has been cancelled. Claims 9 and 19 have been amended to further define what happens to the electrode cartridge after detachment from the main unit. Since no new matter is introduced by these changes, the amendment should be entered at this time.

Claims 1, 3, 5-7, 9, 12-17, 19, 22, and 22-24 have been rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over a publication by Bramson et al. (Gene Therapy 10: 251-260, 2003; referred to hereafter as "Bramson") in view of U.S. Patent No. 6,302,874 to Zhang et al. (referred to hereafter as "Zhang").

Bramson discloses a microporation technique whereby a vaporization process was used to remove tiny areas of the stratum corneum creating microscopic pores that enabled topical immunization using an adenovirus vaccine as a vector for genetic vaccination (see abstract and p. 252, left column of Bramson). Bramson explicitly teaches the properties of replication-defective adenoviruses which make them appealing vectors for genetic vaccination, i.e., they elicit robust cellular and humoral responses, they can accommodate up to 8 kb of foreign DNA, they are easily manipulated and propagated using basic molecular biology and tissue culture techniques, and they have not been associated with disease in immunocompetent hosts (p. 252, left column of Bramson). According to Bramson, microporation is preformed by the contact of electrically heated small-diameter wires with the skin surface. Moreover, the microporation system of Bramson is different from the apparatus of the present invention as it is characterized by the following features: (1) the wires in the microporation system of Bramson are strapped over the edge of a ceramic substrate so that the wires are parallel to the skin surface; and (2) the electrical current passes through the wires only, not through the skin, the wires are heated and thereby generate micropores, namely by thermal ablation. The microporation system of Bramson enables genetic immunization, e.g., against ovalbumin, by using replication defective adenoviruses as vectors for a foreign DNA.

More importantly, claims 1 and 14 as amended now recite that the electrode cartridge is designed for attachment to the main unit and subsequent detachment from the main unit. As shown in Figures 9 and 10 submitted with the Amendment filed on August 28, 2008, the main unit (1) of the apparatus disclosed in the present invention is configured to contain electrical contacts (2) through which the electrical energy from the main unit is transferred to the electrode cartridge (3). Due to this distinct configuration, the electrode cartridge of the present invention is not wire-connected to the main unit, and can be attached before use and detached after use (paragraph [0066] of the published application). In sum, the electrode cartridge of the present invention is not an integral part of the apparatus.

In contrast, Bramson discloses that the tungsten wires are electrically connected to the control circuitry via copper traces (see p. 259, left column of Bramson). Thus, the tungsten wires of Bramson, which the Examiner equates to the electrode cartridge of the present invention, are not detachable from the control circuitry, the main unit, as recited and claimed in claims 1 and 14 as amended. The Examiner is correct in stating that the user of the device of Bramson may remove the set of tungsten wires from the skin surface after creating the micro-pores. However, unlike the presently claimed invention, the set of tungsten wires of Bramson cannot be removed from the control circuit, the main unit. As explained above, the set of tungsten wires in Bramson remains physically connected to the control circuit, the main unit, via copper traces at all times, with no possibility of easy attachment to the main unit and subsequent detachment from the main unit, as recited and claimed in claims 1 and 14 as amended. Therefore, Bramson does not teach or suggest the presently claimed invention.

Zhang does not remedy the deficiencies of Bramson. Zhang teaches apparatuses for electroporation so as to create transient aqueous pathways (pores) in lipid bilayers (col. 2, ll. 65-66; col. 4, ll. 31-33 of Zhang). The apparatus according to Zhang comprises a mini pulse generator in electrical contact with an electrode (col. 10, ll. 30-34 of Zhang). The electroporation according to Zhang is achieved by pulsed electric fields, specifically electrostatic fields (FIG. 2; col. 9, ll. 61-63; col. 10, ll. 1-6; col. 10, ll. 14-16 of Zhang). Zhang further discloses transdermal delivery of L-ascorbic acid for cosmetic treatment of skin conditions (col. 3, ll. 54-61; col. 7, ll. 31-33 of Zhang). Moreover, the delivery of L-ascorbic acid according to Zhang is enhanced by applying an electric pulse having sufficient strength and duration to the composition so as to topically deliver L-ascorbic acid to the region of skin (col. 4, ll. 31-42; col.

7, ll. 10-18 of Zhang). Thus, even if one of ordinary skill in the art at the time the invention was made was to modify the patch of Bramson to a patch containing a cosmetic composition of Zhang, he/she would only obtain a system which comprises a laptop computer, a microprocessor control circuitry, a three-axis stepper motor assembly with microporation tip holder. The microporation tip would comprise small-diameter wires strapped over the edge of a ceramic substrate and electrically connected to the control circuitry, which would allow for the control of the electrical current pulses to pass through the wires and heat the wires. As a result, the wires would heat up the skin surface and create lines of micropores on the patient's skin. The patch of Zhang comprising L-ascorbic acid would then be applied onto the skin where micropores are present. Thus, even combining the Bramson system with the patch of Zhang, one of ordinary skill in the art would not arrive at the presently claimed system, which comprises, *inter alia*, an electrode cartridge designed for easy attachment to the main unit and subsequent detachment from the main unit, because neither reference teaches or suggests this feature. In sum, claims 1 and 14 as well as their dependent claims 5-7, 9, 12, 13, 15-17, 19 and 22-24 are patentable over Bramson in view of Zhang. Therefore, the rejection over Bramson in view of Zhang should be withdrawn.

Claim 4 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Bramson in view of Zhang and further in view of U.S. Patent Application Publication No. 2002/0010414 to Coston (referred to hereafter as "Coston"). As explained above, the combination of Bramson and Zhang does not teach or suggest the presently claimed invention. Coston appears to be cited as an attempt to remedy the failure of Bramson and Zhang to teach that the electrical energy is of radio frequency.

However, Coston does not remedy the deficiencies of Bramson in view of Zhang. Coston discloses methods and devices for transporting a molecule through a mammalian barrier membrane through electroperforation of the membrane. Coston teaches various apparatuses for the electroperforation methods, one of which comprises a housing, a current generator, a current controller, and a treatment electrode for electroperforation in a mono-terminal operation (*see* paragraph [0067] and FIG. 1 of Coston). The electric current according to Coston is driven from the treatment electrode to the membrane, and optionally to the indifferent electrode (*see* paragraph [0015] of Coston). The electric current may be a direct current or an alternating current. The frequency of the alternating current may be between 30 Hz to 10,0000 kHz (*see*

paragraph [0016] of Coston). In operation, the current generator and the current controller, in communication with the treatment electrode, provide an electric current to the treatment electrode (FIG. 1 and paragraph [0068] of Coston). Coston further teaches a "roller-like" and a "stamp-like" devices which comprise a handle that comprises an electric current controller and an electric current generator (FIG. 6 and paragraphs [0088] and [0090] of Coston). The arms of the apparatus comprise the connecting wires allowing electric communication between the current controller and current generator in the handle and the electrode array on the roller or on the flat surface (paragraphs [0088] and [0090] of Coston). The treatment electrodes and the electrode array in the electroperforation apparatuses disclosed by Coston are all electrically connected by connecting wires to the current generator and to the current controller allowing electric communication between the current generator, the current controller and the treatment electrodes (explicitly exemplified and depicted in FIGs. 1 to 4 of Coston). The treatment electrodes and the electrode array disclosed by Coston are an integral part of the electroperforation apparatuses, their height in some of the apparatuses may be adjusted relative to the tissue, but they are not detached or removed from the apparatuses, in contrast to claims 1 and 14 as amended, which now recite and claim that the electrode cartridge is designed for easy attachment to the main unit and subsequent detachment from the main unit. Thus, even combining the Bramson system with the patch of Zhang and the frequency parameter of Coston, one of ordinary skill in the art would not arrive at the system recited in claim 4, which comprises, *inter alias*, an electrode cartridge designed for easy attachment to the main unit and subsequent detachment from the main unit, because none of the cited references teaches or suggests this feature. Therefore, the rejection of claim 4 over Bramson in view Zhang, and further in view of Coston should be withdrawn.

Claims 8, 10, 11, 18, 20, and 21 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Bramson in view of Zhang, and further in view of U.S. Patent No. 6,477,410 to Henley (referred to hereafter as "Henley"). As explained above, the combination of Bramson and Zhang does not teach or suggest the presently claimed invention. Henley appears to be cited as an attempt to remedy the failure of Bramson and Zhang to teach wherein the cosmetic agent is hydroquinone.

However, Henley does not remedy the deficiencies of Bramson in view of Zhang. Henley teaches a self-powered hand-held electrokinetic delivery device for self-administering a

medicament. The hand-held device of Henley electrokinetically drives the medicament from an applicator into the treatment site (col. 6, ll. 50-54 of Henley). Henley discloses different medicaments including hydroquinone and antibacterial agents to be delivered electrokinetically. However, Henley does not teach or suggest an apparatus comprising, *inter alia*, an electrode cartridge designed for easy attachment to the main unit and subsequent detachment from the main unit. Thus, even modifying the Bramson system with the patch of Zhang to apply the cosmetic agent hydroquinone as taught by Henley, one of ordinary skill in the art at the time the invention was made would not arrive at the presently claimed invention. Therefore, the rejection of claims 8, 10, 11, 18, 20 and 21 over Bramson in view of Zhang, and further in view of Henley should be withdrawn.

Accordingly, it is believed that the entire application is in condition for allowance, early notice of which would be appreciated. Should the Examiner not agree, then a personal or telephonic interview is respectfully requested to discuss any remaining issues and expedite the eventual allowance of this application.

Respectfully submitted,

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